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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,069	04/04/2001	Yaakov Naparstek	56040-B/JPW/GJG/CSN	3884

7590 01/30/2006

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/826,069	NAPARSTEK, YAAKOV	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 11/18/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendments, remarks, filed 11/18/05, have been entered.

2. Claim 8-10 are being acted upon.

3. As set forth previously, the priority date of the instant application is its filing date, 4/04/2001.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 8-10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gaubitz et al. (1999) in view of U.S. Patent No. 6,228,363 and Madaio et al. (1996).

As set forth previously, Gaubitz, M., et al. teaches a method of treating lupus comprising extracorporeal column immunoadsorption of a subject's plasma for the removal of pathogenic antibodies. The reference further teaches that dsDNA-Ab play a "pivotal" role in the pathogenesis of SLE and that their removal proved useful for the treatment of the disease (see particularly Introduction and Discussion).

The reference teaching differs from the claimed invention only in that it does not teach a method employing a column comprising the R38 peptide nor the use of a Sepharose™ column.

The '363 patent teaches that the R38 peptide is derived from laminin and is recognized by pathogenic lupus antibodies (see particularly column 3, lines 13-19).

Madaio et al. teaches that dsDNA-Ab from lupus patients also recognize laminin (see particularly Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of treating lupus comprising extracorporeal column immunoadsorption of a subject's plasma for the removal of pathogenic antibodies, as taught by Gaubitz et al., employing the R38 peptide of the '363 patent. One of ordinary skill in the art at the time the invention was made would have been motivated to employ the R38 peptide on an immunoadsorption column given the teachings of Madaio et al. that dsDNA-Ab from lupus patients also recognize laminin and the '363 patent that the R38 peptide is derived from laminin and is recognized by pathogenic lupus antibodies. Note that Claim 8 is included in the rejection because various types of immunoadsorber matrices (including Sepharose™) for column chromatography were well-known in the art at the time of the invention. The choice of any particular immunoadsorber matrix would have comprised only routine optimization of the claimed method and would have been well within the purview of one of ordinary skill in the art at the time of the invention. Note that new claim 10 does not recite any new limitations because all ligands are coupled to Sepharose™ in some sort of "coupling buffer" (an ordinarily skilled artisan would know that Sepharose™ could not used in a dry form for column chromatography because column chromatography employs the flow of liquid through the column).

Applicant's arguments, filed 11/18/05, have been fully considered but they are not persuasive. Applicant again argues against the references individually.

Applicant is again reminded that it is the combination of references, in further view of the knowledge of the ordinarily skilled artisan, upon which the rejection is based.

As part of an argument that there is no motivation to combine the references, Applicant specifically argues that Madaio et al. teaches away from the claimed invention with the teaching that "serum autoantibody levels frequently do not correlate with disease activity", and thus, cannot be used for motivation to combine the references.

This statement would seem to have been considered somewhat out of context. The statement is found in what could be considered the background section of the reference. The paper more specifically addresses autoantibody involvement in lupus nephritis. In a section entitled "DIRECT INTERACTIONS OF AUTOANTIBODIES WITH GLOMERULAR ANTIGENS", the reference states, "we and others have observed that nephritogenic lupus autoantibodies cross-reacted with glomerular basement membrane and cell surface constituents, including … laminin". In the section entitled "LOCALIZATION OF AUTOANTIBODIES WITHIN LIVING CELLS", the reference goes on to teach, "Cell-surface binding appears to be an important initial step for cellular entry of anti-DNA antibodies that negotiate both

cell and nuclear membranes to localize within the nucleus". Clearly, in this instance, there exists every expectation that autoantibodies do correlate with disease activity.

Applicant argues that antibodies that bind to laminin cannot be presumed to bind the R38 peptides.

It is well-established that for whatever reason, antibodies to peptides routinely bind the proteins comprising the same sequence, regardless, the '363 patent teaches that the R38 peptide is indeed recognized by lupus autoantibodies.

Applicant argues that the binding of an antibody to a peptide on a plate in an ELISA test does not mean the same peptide will successfully bind the same antibody when the peptide is attached, for example to a Sepharose™ bead.

Applicant is advised that antibody ligands have been routinely attached to Sepharose™ beads for 30+ years prior to the filing date of the instant application, see for example, Cuatrecacas et al. (1969). A Medline search of "Sepharose™ and antibody and peptide" yields 1600+ hits. Clearly, the concept of attachment of ligands to Sepharose™ for the removal of a particular antibody from a solution would have been a concept well-known to the ordinarily skilled artisan at the time of the invention.

Applicant again argues unpredictable results in removing 30-60% of the pathogenic antibodies from the plasma of an SLE patient (Example 12). Applicant submits a 1.132 declaration of Inventor Naparstek in support.

As set forth previously, the experiments of Gaubitz et al. show that up to 70% of the antibodies could be removed from an SLE patient's plasma sample. Thus, the results would not appear to be unpredictable Regardless, an argument of unexpected results employing post-filing data, e.g., the instant declaration of Inventor Naparstek is improper as unexpected results must be set forth in the specification. Further, unexpected results are considered to be a secondary consideration, the arguing of which indicates an admission that an invention is indeed obvious but patentable in view of the unexpected results. Accordingly, this argument seems inconsistent with

Applicant's argument that the invention of the instant claims is not obvious.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

8. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

1/24/06

G.R. Ewoldt, Ph.D.
Primary Examiner
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